CHOATE

CHOATE HALL & STEWART LLP

March 26, 2008

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BY ELECTRONIC FILING

The Honorable Douglas P. Woodlock
UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS
John Joseph Moakley U.S. Courthouse
One Courthouse Way, Suite 4110
Boston, Massachusetts 02210

Re: John Hancock Life Insurance Company, *et al.*
v. Abbott Laboratories
U.S.D.C. (Mass.) Civil Action No. 05-11150-DPW

Dear Judge Woodlock:

During the live cross-examination of Dr. John Leonard on Tuesday, March 11, 2008, Your Honor requested that John Hancock provide the Court with a reference to "Abbott documents that predate [the Research Funding Agreement]" demonstrating Abbott's knowledge that Phase III development of "Prinomastat" and "Marimastat," two competing MMPI compounds in the same family as ABT-518, previously had been discontinued by their respective sponsors, contrary to the express representations made by Abbott on pages 4-5 of its final Descriptive Memorandum for ABT-518 (Trial Exhibit No. 265). *See* Trial Tr. vol. 1, pp. 1013-1014 (March 11, 2008), relevant excerpts of which are attached hereto as Exhibit A.

In response to Your Honor's request, John Hancock respectfully refers the Court to Trial Exhibit Nos. 196, 308 and 67, copies of which are also attached to this letter for the Court's convenience. As represented on March 11, 2008, each of these exhibits predates the signing of the Research Funding Agreement, and each demonstrates Abbott's knowledge prior to March 13, 2001 that Phase III clinical development of Prinomastat and/or Marimastat had been discontinued.

More specifically, Exhibit 196 is an internal Abbott e-mail, dated August 7, 2000, circulating a Pfizer press release, dated August 4, 2000, which announced, in part, on page ABBT0061748 that,

> Pfizer halted phase III clinical trials of prinomastat, a matrix metalloprotease inhibitor, in advanced hormone refractory cancer and advanced non-small cell lung cancer, on failure

> to meet primary efficacy objectives. The company intends to continue exploration of prinomastat in other tumor types and in earlier stage disease. Pfizer said four phase II trials are currently underway and two additional phase II trials will begin shortly.

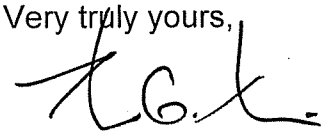
Exhibit 308 is an internal Abbott document titled "July 2000 - 'Top' Issues," which states, in part, on page ABBT0017616 that "Pfizer (Agouron) announced 8/4/00 that they were stopping Phase III trials of prinomastat in advanced prostate and NSCLC [*i.e.*, non-small cell lung cancer] because 'primary efficacy objectives were not met.'"

Lastly, Exhibit 67 is an internal Abbott monthly update concerning ABT-518, dated February 2001, which repeats on page ABBT0000345 that "Pfizer announced 8/4/00 that they were stopping Phase III trials of prinomastat in advanced prostate and NSCLC because 'primary efficacy objectives were not met,'" and further states on the same page that "Marimastat development was discontinued on 2/15/01" by "British Biotech."

I hope that these materials provide the information that Your Honor was seeking. If for some reason they do not, I would be happy to respond further if instructed to do so by the Court.

Thank you for your consideration.

Very truly yours,



Brian A. Davis

Attachments

cc: Jeffrey I. Weinberger, Esq. (by electronic mail)
Gregory D. Phillips, Esq. (by electronic mail)
Eric J. Lorenzini, Esq. (by electronic mail)
Özge Güzelsu, Esq. (by electronic mail)

4314303.1

EXHIBIT A

Q. Do you recall that there was some discussion and some questions by Mr. Weinberger about Marimistat and Prinomastat?

Do you remember that?

A. I do recall.

Q. And I think it was your testimony that -- he showed you some documents that indicated that they were still in -- at least Prinomastat was still in Phase II trials; do you remember that?

A. I do.

Q. In fact, I think it was Plaintiff's BD, now Exhibit 200, and it's in your binder.

Would you take a look at that document for a moment?

A. (The witness so complied.)

(Pause.)

BY MR. DAVIS:

Q. And if you'd look at the second page of Exhibit 200, the page that ends in 9971.

Do you see that?

A. I have that.

Q. Reference at the bottom to Prinomastat, right?

A. Yes.

Q. And it says: Pfizer discontinued the Phase III studies. mentioned above in August of 2000, due to failure to meet primary efficacy objectives.

Do you see that?

A. I do.

Q. You knew, even before this document came down, this was written that Abbott -- that Pfizer had discontinued any Phase III studies for that compound, right?

A. The value of the information we have at ASCO speaks to totally different scientific things that we needed to learn to make an informed decision.

A press release is not the useful way of sharing information that we can make any kind of informed scientific judgment on a product.

Q. But you knew before -- certainly, before the date of this document, and before even March of 2001 -- that Pfizer had stopped all of its Phase III trials for Prinomastat?

THE COURT: Phase II or Phase III?

BY MR. DAVIS:

Q. Phase III trial for Prinomastat.

A. Actually, I don't know that all Phase III trials were

stopped.

We're aware that two were stopped. I don't think we knew how many were actually going on. There was no registry to disclose all the work that was taking place. We knew they continued to be active in the field.

Q. But Abbott represented to Hancock that there were Phase III trials underway, correct, for that compound, right?

A. At that time, yeah.

Q. And Marimistat, I think there were some questions about Marimistat, and Mr. Weinberger directed your attention to the last sentence in that paragraph which states: According to BBT executives, the future direction of Marimistat development is the subject of ongoing discussion with Schering-Plough and with external experts.

Do you see that?

A. Yes, I do.

Q. And, in your mind, Dr. Leonard, is that the same as

saying that Marimistat is still in Phase III trial?

A. I don't know what it means.

Q. And it's true, is it not, Dr. Leonard, that, even after Dr. Leiden reversed the halt on the Phase I clinical trial of ABT-518, in March of 2001, that other development activities for that compound remained on hold?

A. I think that's true.

Development is an array of different things that

take place. Clinical trials and much of development is not clinical trials. Formulation development, toxicology, statistical plans, et cetera.

Things that are necessary for Go/No-Go Decisions may be on a critical path, other activities are not on a critical path, and we look all the time to make sure we are doing things in the most efficient cost-effective way, and that's probably what was taking place with that program.

Q. Would you agree with me that when Dr. Leiden issued his halt order in early March of 2001, that the only thing that was restarted afterwards was the Phase I clinical trial, the

other development activities for ABT-518 remained on hold?

A. I don't recall specifically, but that wouldn't surprise me.

That's the key critical information to make a decision and go forward.

THE COURT: May I just stop for a moment?

MR. DAVIS: Yes.

THE COURT: Because I don't understand the aspects of BD, which had been marked as 200, just in terms of timing.

If we turn to Page 971, second page of the memorandum, the two points that you made reference to do have footnotes to them. Starting with Marimistat, the quotation of subject of ongoing discussion with Schering-Plough with external experts is Footnote 10, and that then, refers to some

news release on May 2, 2001?

MR. DAVIS: Yes, Your Honor.

THE COURT: After that decision was made or after the clinical -- or, after the agreement was entered into?

MR. DAVIS: Correct, Your Honor.

THE COURT: That's the source of that information?

MR. DAVIS: Well, Your Honor, there is a February, 2001, document that has been entered in evidence.

THE COURT: But, referring to this document, that's the source?

MR. DAVIS: As I understand it, Your Honor.

THE COURT: Okay; and, turning to the Prinomastat, this first cite, anyway, is -- in the page running over from 971 to 972, is the sentence dealing with the four Phase II trials with, two additional trials planned, and that is a reference report on July 2, 2001, right?

MR. DAVIS: Yes.

THE COURT: Now, is that, do you understand, whether that discontinuance, in August, 2000, was the subject of that reference report or was there some information publicly available before that?

MR. DAVIS: It was information publicly available, and it's represented in Abbott documents that predate this agreement.

THE COURT: Alright. I want to be referred to

those, at some point.

MR. DAVIS: I will do that.

THE COURT: Okay.

EXHIBIT 196

Susan M Glad/LAKE/PPRD/ABBOTT
10/19/2000 11:44 AM

To Diane L D'Amico/LAKE/PPRD/ABBOTT@ABBOTT
cc
bcc
Subject Toxicology Comments on ABT-518 Strategy

Diane:

I know that this is a lot of information but it might serve as a useful archive at some point

Sue

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------

William M Bracken
05/22/2000 09:46 AM

To: Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT
cc: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT
Subject: Toxicology Comments on ABT-518 Strategy

Bob

My comments are attached and are in red

Bill

ABT-518 Strategy v2.do

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------

Steve Wittenberger
05/25/2000 01:02 PM

To: Azmi A Nabulsi/LAKE/PPRD/ABBOTT@ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, William M Bracken/LAKE/PPRD/ABBOTT@ABBOTT, John F Bauer/LAKE/PPRD/ABBOTT@ABBOTT, Kennan C Marsh/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Steven K Davidsen/LAKE/PPRD/ABBOTT@ABBOTT
cc: Steve King/LAKE/PPRD/ABBOTT@ABBOTT, Clint Brooks/LAKE/PPRD/ABBOTT@ABBOTT, David R Hill/LAKE/PPRD/ABBOTT@ABBOTT, Ashok K Gupta/LAKE/PPRD/ABBOTT@ABBOTT, Sou-Jen Chang/LAKE/PPRD/ABBOTT@ABBOTT, James A Morley/LAKE/PPRD/ABBOTT@ABBOTT, Thomas P Eskay/LAKE/PPRD/ABBOTT@ABBOTT, Dilinie P Fernando/LAKE/PPRD/ABBOTT@ABBOTT, Dilinie P Fernando/LAKE/PPRD/ABBOTT@ABBOTT
Subject: MMPI ABT-518

This is to update the progress of the campaign to prepare ABT-518 for toxicological and phase one multiple dose studies. The synthesis is proceeding very well. We have experienced problems and delays in the delivery of key starting materials that have put us off our original delivery estimates, however we are now past those points. This campaign should deliver approximately 5kg bulk drug (although I caution that it is not yet "in the bottle").

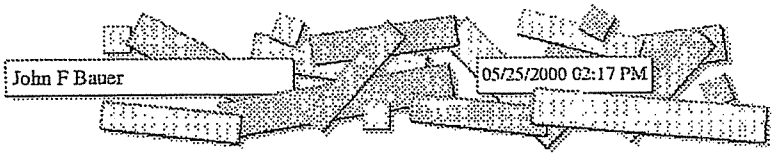
At this point the estimate is 1.5kg will be required to supply the 1-month tox studies and this material should be ready by Friday June 16. We are scheduled to move into the R8 facility the week of June 26 to process the material needed to support the first part of the clinical study. This material will done by June 30 at which point it will move to PARD for analysis and approval. The plan is to deliver enough bulk drug to prepare all of the 25mg doses as well as sufficient compound to make 200mg doses to take us into 2Q 2001. Approximate amounts of total compound required to take us through the following months are April, 900g; May, 1300g; June, 1800g. A decision on exactly when to plan the resupply depends somewhat on other bulk drug needs, stability data, etc., and will need to be made shortly. Any drug not used for the tox studies or the clinical study would be available for other uses (such as formulation etc.).

We are finishing up gathering quotes on raw materials to provide cost estimates on 5kg and 30kg bulk drug deliveries to provide material for the rest of the phase one study and beyond. The numbers will be presented as soon as they are available.

I'd like to aknowledge the tremendous efforts of the Process Chemistry/PARD MMPI team: Sou-Jen Chang, Dilinie Fernando, David Hill, Ashok Gupta, Tom Eskay, and Jim Morley. They have done a great job in defining and executing the synthetic chemistry on scale and developing methods and identifing impurities on the analytical side. Thanks to the rest of the transistion team as well for bearing with us through the slow times of the scale-up campaign as we waited for our materials to be delivered.

SJW

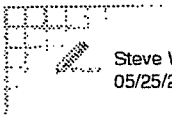
---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------



To: Steve Wittenberger/LAKE/PPRD/ABBOTT@ABBOTT
cc: Azmi A Nabulsi/LAKE/PPRD/ABBOTT@ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, William M Bracken/LAKE/PPRD/ABBOTT@ABBOTT, Kennan C Marsh/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Steven K Davidsen/LAKE/PPRD/ABBOTT@ABBOTT, Steve King/LAKE/PPRD/ABBOTT@ABBOTT, Clint Brooks/LAKE/PPRD/ABBOTT@ABBOTT, David R Hill/LAKE/PPRD/ABBOTT@ABBOTT, Ashok K Gupta/LAKE/PPRD/ABBOTT@ABBOTT, Sou-Jen Chang/LAKE/PPRD/ABBOTT@ABBOTT, James A Morley/LAKE/PPRD/ABBOTT@ABBOTT, Thomas P Eskay/LAKE/PPRD/ABBOTT@ABBOTT, Dilinie P Fernando/LAKE/PPRD/ABBOTT@ABBOTT, Yeshwant D Sanzgiri/LAKE/PPRD/ABBOTT@ABBOTT, John B Cannon/LAKE/PPRD/ABBOTT@ABBOTT
Subject: Re: MMPI ABT-518

Thanks for the update Steve. The information about the formulations is correct at this point but we would much prefer to do 50 mg rather than 25 mg if tox permits. Bob and Bill please let us know as soon as you can. thanks

Steve Wittenberger



Steve Wittenberger
05/25/2000 01:02 PM

To: Azmi A Nabulsi/LAKE/PPRD/ABBOTT@ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, William M Bracken/LAKE/PPRD/ABBOTT@ABBOTT, John F Bauer/LAKE/PPRD/ABBOTT@ABBOTT, Kennan C Marsh/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Steven K Davidsen/LAKE/PPRD/ABBOTT@ABBOTT

cc: Steve King/LAKE/PPRD/ABBOTT@ABBOTT, Clint Brooks/LAKE/PPRD/ABBOTT@ABBOTT, David R Hill/LAKE/PPRD/ABBOTT@ABBOTT, Ashok K Gupta/LAKE/PPRD/ABBOTT@ABBOTT, Sou-Jen Chang/LAKE/PPRD/ABBOTT@ABBOTT, James A Morley/LAKE/PPRD/ABBOTT@ABBOTT, Thomas P Eskay/LAKE/PPRD/ABBOTT@ABBOTT, Dilinie P Fernando/LAKE/PPRD/ABBOTT@ABBOTT, Dilinie P Fernando/LAKE/PPRD/ABBOTT@ABBOTT
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SJW

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------

Robert Hansen
06/15/2000 12:09 PM

To: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, Lori V Rountree/LAKE/PPRD/ABBOTT@ABBOTT, Azmi A Nabulsi/LAKE/PPRD/ABBOTT@ABBOTT, Diane C Bronson/LAKE/PPRD/ABBOTT@ABBOTT
cc:
Subject: ABT-518 tox lot

---------- Forwarded by Robert Hansen/LAKE/PPRD/ABBOTT on 06/15/2000 12:08 PM ----------

STEVEN WEINBERGER
06/15/2000 11:11 AM

To: William M Bracken/LAKE/PPRD/ABBOTT@ABBOTT, Lise I Loberg/LAKE/PPRD/ABBOTT@ABBOTT

cc: James A Morley/LAKE/PPRD/ABBOTT@ABBOTT, Thomas P Eskay/LAKE/PPRD/ABBOTT@ABBOTT, John F Bauer/LAKE/PPRD/ABBOTT@ABBOTT, Steve King/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Steven K Davidsen/LAKE/PPRD/ABBOTT@ABBOTT, Perry D Nisen/LAKE/PPRD/ABBOTT@ABBOTT
Subject: ABT-518 tox lot

We have completed preparing the tox lot of ABT-518. 1.70kg of the material (lot# 67304-147-4) will be sent to Bill Bracken via the stockroom shuttle this afternoon. Analytical results will be forthcoming from Jim Morley.

We have about 4kg that will been processed in the CAPD R8 special labs the week of June 26 that will be available for clinical use following analytical evaluation and release.

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------

Robin A Rothkopf
06/16/2000 08:59 AM

To: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Rebecca S Hoffman/LAKE/PPRD/ABBOTT@ABBOTT, Azmi A Nabulsi/LAKE/PPRD/ABBOTT@ABBOTT
cc:
Subject: MMPI press release

Decision Resources Study Evaluates the Clinical Progress and Commercial Potential of Emerging Matrix Metalloproteinase Inhibitors

---

Date: Thursday, June 15, 2000
Source: PR Newswire

WALTHAM, Mass., June 14 /PRNewswire/ via NewsEdge Corporation -- Data from extensive experimental research and clinical studies provide strong evidence suggesting that matrix metalloproteinases (MMPs) are intimately involved in physiological processes of tissue remodeling and development. Matrix metalloproteinase inhibitors (MMPIs) are being developed for various forms of cancer, arthritis (osteoarthritis and rheumatoid arthritis), periodontal diseases, and ocular diseases. Laboratory and clinical studies have established that MMPIs are orally active and, apart from possible musculoskeletal side effects, well tolerated compared with many of the drugs with which they will have to compete (e.g., cytotoxics and corticosteroids). Assuming MMPIs prove efficacious in ongoing clinical trials, their advantages will support the widespread use of these drugs, mainly for treating cancer and arthritis.

(Photo: http://www.newscom.com/cgi-bin/prnh/20000303/DECISION)

Emerging Matrix Metalloproteinase Inhibitors is a new study published by Decision Resources, Inc that presents a thorough review of the roles of MMPs in biology and disease, placing a major emphasis on the development of MMPIs . This study is based on in -depth interviews with researchers active in MMPI development and presents their views regarding the key issues involved in the successful commercialization of these agents . The relative merits of each MMPI are analyzed with respect to their market potential, as well as their ability to compete with existing therapies . An assessment of the most prominent pharmaceutical companies with significant MMPI development programs is also presented.

We project that sales of MMPIs for six major cancers (breast, non-small- cell lung, small-cell lung, prostate, ovarian, and colorectal) will generate sales of nearly $900 million by 2009, assuming positive results in ongoing trials. The main factor that may limit future sales of MMPIs for cancer is the wealth of competing antiangiogenesis agents being developed, of which several appear promising

In the arthritis market, MMPIs face different challenges, particularly musculoskeletal side effects. However, considerable progress has been made in this area and we believe that the earlystage MMPIs with improved side-effect profiles will succeed in the clinic. Assuming use in only a small fraction of early-stage patients we estimate sales of MMPIs for arthritis will reach $1.3 billion by 2009-an impressive return for companies willing to venture into this "high-risk" arena.

Emerging Matrix Metalloproteinase Inhibitors is part of Mosaic, one of six Pharmacor services that evaluate the commercial potential of drugs in research and development

Contact: Frank Sama, 781.487.3753 (telephone), 781.487.5750 (fax), or sama@dresources.com (e-mail).
In Europe, contact Ms. Vera Bisegna, +32.2.351.1079 (telephone), +32.2.351.2347 (fax), or vbisegna@compuserve.com (e-mail).
In Japan, contact Ms. Makiko Yoshimoto, +81.3.5401.2615 (telephone), +81.3.5401.2617 (fax), or makiko@bl.mmtr.or.jp (e-mail). http://www.dresources.com

Decision Resources, Inc., is a world leader in research publications, advisory services, and consulting designed to help clients shape strategy,
allocate resources, and master their chosen markets. Founded as a subsidiary of Arthur D. Little, Inc., the company has provided strategic information
services for 30 years, assessing industry trends in the international health care and pharmaceutical industries.

SOURCE Decision Resources, Inc.

/CONTACT: Frank Sama of Decision Resources, 781-487-3753,
or sama@dresources.com/ /Photo: NewsCom:
http://www.newscom.com/cgi-bin/prnh/20000303/DECISION AP Archive: http://photoarchive.ap.org PRN Photo Desk,
888-776-6555 or 201-369-3467/ /Web site: http://www.dresources.com/

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------

Steven K Davidsen 06/16/2000 09:21 AM

To: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Perry D Nisen/LAKE/PPRD/ABBOTT@ABBOTT
cc:
Subject: Re: MMPI press release

I forwarded an earlier version of this to Lisa last week - she thinks the numbers are a bit high

Steve
Susan M Glad

Susan M Glad
06/16/2000 09:12 AM

To: Lisa A Lux/LAKE/PPD/ABBOTT@ABBOTT, Steven K Davidsen/LAKE/PPRD/ABBOTT@ABBOTT, Lori V Rountree/LAKE/PPRD/ABBOTT@ABBOTT, Diane C Bronson/LAKE/PPRD/ABBOTT@ABBOTT, Diane M Medina/LAKE/PPRD/ABBOTT@ABBOTT, Kysa A Meek/LAKE/PPRD/ABBOTT@ABBOTT, Karla Fischer/LAKE/PPRD/ABBOTT@ABBOTT
cc: Azmi A Nabulsi/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Rebecca S Hoffman/LAKE/PPRD/ABBOTT@ABBOTT
Subject: MMPI press release

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 06/16/2000 09:11 AM ----------

Robin A Rothkopf
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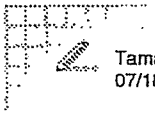
SOURCE Decision Resources, Inc.

/CONTACT: Frank Sama of Decision Resources, 781-487-3753, or sama@dresources.com/ /Photo: NewsCom: http://www.newscom.com/cgi-bin/prnh/20000303/DECISION AP Archive: http://photoarchive.ap.org PRN Photo Desk, 888-776-6555 or 201-369-3467/ /Web site: http://www.dresources.com/

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------



Tamara L Garavalia
07/18/2000 03:29 PM

To: Kysa A Meek/LAKE/PPRD/ABBOTT@ABBOTT
cc: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, John B Cannon/LAKE/PPRD/ABBOTT@ABBOTT
Subject: Re: MMP CSR drug needs

Kysa,

Attached is the Bulk CSR as discussed:


OTV00 3110.doc

Please fax a copy of the approved Bulk CSR to me at 78253. Send the original to John Cannon 4P7 R1B.

Regards,
Tamara
Kysa A Meek

Kysa A Meek

07/18/2000 01:02 PM

To: Tamara L Garavalia/LAKE/PPRD/ABBOTT@ABBOTT
cc: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT
Subject: MMP CSR drug needs

Tamara,

Here are the numbers I have come up with for the MMPI study:

For the entire study we need:

10060 25 mg capsules (this gives us flexibility in case we need to decrease the dosing intervals to 50 mg)
17888 200 mg capsules

If we have drug available to ship in May we need the following with this supply:

7125 25 mg capsules
3188 200 mg capsules

If we don't have drug available to ship until August we need:

8175 25 mg capsules
7276 200 mg capsules

If you could send me the CSR today I can sign it – otherwise Susan will have to sign it because I am leaving for vacation tomorrow. When you get a chance, give me a call and we can call the PARD folks.

Thanks again for your help,

Kysa

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------

Kysa A Meek

07/18/2000 03:29 PM

To: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT

cc:
Subject: MMP CSR

Sue,

I will send the CSR to John this afternoon. Here is the scoop. They are going to make 6000 25 mg capsules now. They won't be able to make the entire 10060 at once. They will make 200 mg capsules in December. They never were going to make 200 mg caps now. I told Tamara to get in touch with you if she needs anything else.

Kysa
---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM

Robert Hansen
07/19/2000 07:59 AM

To: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT
cc:
Subject: Re: MMP CSR

Susan

Did Kysa calculate her numbers from the supply spread sheet on the L: drive?

Bob
---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM

Janice A Schroeder 07/21/2000 09:05 AM

To: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, Diane C Bronson/LAKE/PPRD/ABBOTT@ABBOTT
cc:
Subject: CDA - Dr. Zonnenberg

I received the signed, faxed CDA from Dr. Zonnenberg this morning.
---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM

Robin A Rothkopf
08/07/2000 08:15 AM

To: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, Azmi A Nabulsi/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Lori V Rountree/LAKE/PPRD/ABBOTT@ABBOTT
cc:
Subject: MMPI press release

Pfizer halted phase III clinical trials of prinomastat, a matrix metalloprotease inhibitor, in advanced hormone refractory prostate cancer and advanced non -small cell lung cancer, on failure to meet primary efficacy objectives .

Date: Monday, August 7, 2000
Source: Bridge Information Systems, Inc.

Bridge Information Systems, Inc. via NewsEdge Corporation : By BridgeNews

New York--Aug 4--Pfizer halted phase III clinical trials of prinomastat, a matrix metalloprotease inhibitor, in advanced hormone refractory prostate cancer and advanced non-small cell lung cancer, on failure to meet primary efficacy objectives. The company intends to continue exploration of prinomastat in other tumor types and in earlier stage disease. Pfizer said four phase II trials are currently underway and two additional phase II trials will begin shortly.

--Rajendra Palande, BridgeNews

The following is the text of today's announcement with emphasis added by BridgeNews BridgeStation links to company data have been inserted at the end: Pfizer Discontinues Phase III Trials of Prinomastat in Advanced Cancers but

NEW YORK and LA JOLLA, Calif., August 4 -- PFIZER (NYSE: PFE) ANNOUNCED TODAY THAT PRELIMINARY RESULTS OF PHASE III CLINICAL TRIALS OF PRINOMASTAT, A MATRIX METALLOPROTEASE INHIBITOR (MMPI), IN ADVANCED HORMONE REFRACTORY PROSTATE CANCER AND ADVANCED (STAGE IV) NON-SMALL CELL LUNG CANCER DID NOT MEET PRIMARY EFFICACY OBJECTIVES. NEITHER DETRIMENTAL NOR CONVINCING BENEFICIAL EFFECT OF THE COMBINATION OF PRINOMASTAT WITH STANDARD CHEMOTHERAPY WAS OBSERVED. CONSEQUENTLY, PFIZER IS HALTING THESE TWO PHASE III TRIALS.

Based on input from the Data Safety Monitoring Board (DSMB), patients having earlier stage (Stage IIIB) disease recruited into a second on-going non-small cell lung cancer trial will continue to be studied. THE COMPANY INTENDS TO CONTINUE EXPLORATION OF PRINOMASTAT IN OTHER TUMOR TYPES AND MOST IMPORTANTLY, IN EARLIER STAGE DISEASE, WHERE ONCOLOGISTS BELIEVE INHIBITION OF ANGIOGENESIS MAY HAVE GREATER UTILITY. FOUR PHASE II TRIALS ARE CURRENTLY UNDERWAY AND TWO ADDITIONAL PHASE II TRIALS WILL BEGIN SHORTLY.

Pfizer conducted multi-center, randomized, double-bind, placebo controlled trials to evaluate the safety and efficacy of prinomastat in combination with standard chemotherapy in patients with advanced hormone refractory prostate cancer and non-small cell lung cancer. Safety was not a factor in the decision to halt these trials. The details of the trial results will be presented on a later date in a scientific forum.

"Although we are disappointed in the outcome of these trials, we intend to continue exploration of prinomastat, and remain very interested in the field of MMPI research, and are committed to the many novel approaches to the treatment of cancer under development in our laboratories. The Phase II clinical trials of prinomastat underway and planned in different tumor settings and earlier stage disease should provide critical information relative to earlier intervention of angiogenesis,"
said Barry Quart, Pharm.D., Head of Pfizer Global Research and Development, La Jolla Laboratories.

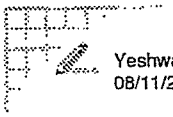
Pfizer Global Research and Development, La Jolla Laboratories is the Research and Development component of Agouron, a wholly owned entity of Pfizer Inc (NYSE: PFE), and are committed to the discovery, development, and marketing of innovative therapeutic products engineered to inactive proteins that play key roles in cancer, AIDS, and other serious diseases.

Pfizer Inc, the world's largest pharmaceutical company, discovers, develops, manufactures and markets leading prescription medicines, for humans and animals, and many of the world's best known over-the-counter brands. This year, Pfizer expects global sales of more than $31 billion and has a research and development
budget of $4.7 billion.

SOURCE Pfizer Inc

/CONTACT: Sonia Anchundo, La Jolla, 858-622-7340, Andy McCormick,212-573-1226, both of Pfizer Inc/

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------



Yeshwant D Sanzgiri
08/11/2000 11:27 AM

To: Thomas P Eskay/LAKE/PPRD/ABBOTT@ABBOTT, John F Bauer/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, Elisabeth A Piquet/LAKE/PPRD/ABBOTT
cc: Stephen I Rynkiewicz/LAKE/PPRD/ABBOTT@ABBOTT, Syndy Herner, John B Cannon/LAKE/PPRD/ABBOTT@ABBOTT
Subject: MMPI (ABT-518) Clinical manufacture - URGENT REQUESTS !!

All,

We are trying to get the MMPI clinical manufacture started on Monday 8/14/00.

We have specific requests for each of you to help make this happen

Tom/John
We need your help to expedite (push!) the physical transfer of bulk drug from the CAPD warehouse to IMM in M3B-2.

Bob/Sue
We need you to approve the Material Release Request as soon as you get it from Syndy Herner of IMM

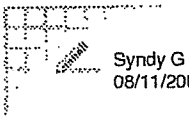
Elisabeth
Can you release 8000 capsules from the 124000 you have placed on hold?
If not we would have to request them from somewhere else and it may take several days and delay us
Many thanks !

All, please call Steve Rynkiewicz at 8-6674 for any updates or clarification. I will be out of the office the minute I send this e-mail !

Thank you,

Yeshwant

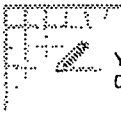
---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------



Syndy G Herner
08/11/2000 11:56 AM

To: Yeshwant D Sanzgiri/LAKE/PPRD/ABBOTT@ABBOTT
cc: Thomas P Eskay/LAKE/PPRD/ABBOTT@ABBOTT, John F Bauer/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, Elisabeth A Piquet/LAKE/PPRD/ABBOTT, Stephen I Rynkiewicz/LAKE/PPRD/ABBOTT@ABBOTT, Syndy G Herner/LAKE/PPRD/ABBOTT@ABBOTT, John B Cannon/LAKE/PPRD/ABBOTT@ABBOTT
Subject: Re: MMPI (ABT-518) Clinical manufacture - URGENT REQUESTS !!

I faxed the release to the venture (87139) this morning. Elisabeth said she does not need the capsules anymore. So, all we need is the drug to arrive in IMM and we will be able to process the bill of material on Monday morning.
Syndy
Yeshwant D Sanzgiri



Yeshwant D Sanzgiri
08/11/2000 11:27 AM

To: Thomas P Eskay/LAKE/PPRD/ABBOTT@ABBOTT, John F Bauer/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, Elisabeth A Piquet/LAKE/PPRD/ABBOTT
cc: Stephen I Rynkiewicz/LAKE/PPRD/ABBOTT@ABBOTT, Syndy Herner, John B Cannon/LAKE/PPRD/ABBOTT@ABBOTT
Subject: MMPI (ABT-518) Clinical manufacture - URGENT REQUESTS !!

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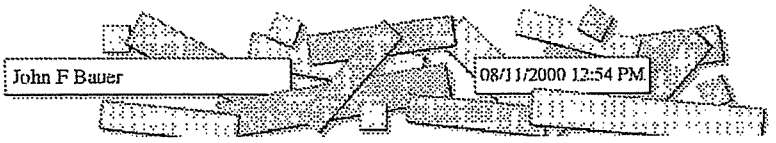
Many thanks !

All, please call Steve Rynkiewicz at 8-6674 for any updates or clarification. I will be out of the office the minute I send this e-mail !

Thank you,

Yeshwant

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------



To: Yeshwant D Sanzgiri/LAKE/PPRD/ABBOTT@ABBOTT
cc: Thomas P Eskay/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, Elisabeth A Piquet/LAKE/PPRD/ABBOTT@ABBOTT, Stephen I Rynkiewicz/LAKE/PPRD/ABBOTT@ABBOTT, Syndy G Herner/LAKE/PPRD/ABBOTT@ABBOTT, John B Cannon/LAKE/PPRD/ABBOTT@ABBOTT
Subject: Re: MMPI (ABT-518) Clinical manufacture - URGENT REQUESTS !!

I checked on the bulk lot and it was sent to IMM this morning. thanks
---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM

Robert Hansen
08/14/2000 09:53 AM

To: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT
cc:
Subject: MMPI Stategy Doc

Susan

For your perusal & on to Sir Nisen

Bob

ABT-518 Strategy.doc
---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM

Tawakol A El-Shourbagy
08/14/2000 01:20 PM

To: Susan M Glad/LAKE/PPRD/ABBOTT
cc: Robert Hansen/LAKE/PPRD/ABBOTT, Azmi A Nabulsi/LAKE/PPRD/ABBOTT@ABBOTT, Dean Hickman/LAKE/PPRD/ABBOTT@ABBOTT, Stanley A Roberts/LAKE/PPRD/ABBOTT, Kennan C Marsh/LAKE/PPRD/ABBOTT, Matthew J Rieser/LAKE/PPRD/ABBOTT@ABBOTT, Reid Patterson/LAKE/PPRD/ABBOTT
Subject: Method Development and Validation for ABT-518 and Metabolites

Sue,

I would like to set up a meeting to discuss the current status of the method for ABT-518 and metabolites. The analytical method for few of the inactive metabolites is turning to be challenging to be validated. I would like to discuss with you the challenges, and see the options that might be available for us to assay the tox. samples for ABT-518 and selected metabolites.

Thanks
---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM

Kysa A Meek

08/15/2000 04:27 PM

To: Jan Peter de Geus/HOOFDDORP/AI/ABBOTT
cc: Jim Looman/HOOFDDORP/AI/ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT
Subject: MMP questions

Jan Peter,

Have you been able to contact Schellens and Zonnenberg regarding the dates of their Ethics Committee meetings in September and October?

We also were wondering about some pharmacodynamic markers and whether or not the sites could perform these assays. The ones we are considering are: VEGF, FGF, TNF1B and IL-8.

Could you send us the essential documents required under the new Dutch law?

Do both of these sites require a signed contract before we can submit everything to the EC?

Thanks in advance for your assistance,

Kysa
---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM

Kysa A Meek

08/18/2000 08:36 AM

To: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, Diane M Medina/LAKE/PPRD/ABBOTT@ABBOTT, Karla Fischer/LAKE/PPRD/ABBOTT@ABBOTT
cc: Robin A Rothkopf/LAKE/PPRD/ABBOTT@ABBOTT
Subject: Re: MMP PD markers

I searched a publication database and I couln't find anything reporting any of these results from clinical trials. That isn't to say they didn't do them, but nothing came up in their results from the trials I looked at

Robin can you try to get this reference for us.

Thanks,

Kysa
---------- Forwarded by Kysa A Meek/LAKE/PPRD/ABBOTT on 08/18/2000 08:33 AM

Steven K Davidsen 08/18/2000 06:02 AM

To: Kysa A Meek/LAKE/PPRD/ABBOTT@ABBOTT
cc: Daniel H Albert/LAKE/PPRD/ABBOTT@ABBOTT, Azmi A Nabulsi/LAKE/PPRD/ABBOTT@ABBOTT
Subject: Re: MMP PD markers

Kysa,

The markers you mentioned have largely been examined in clinical studies with marimastat, prinomastat or BAY 12-9566. Unfortunately, none have particularly useful in predicting efficacious doses. While this may be inherent to the compounds, I suggest that we look beyond what has been tried For example, the latest issue of Clinical Cancer Research (M. Ikeda, volume 6, pp. 3290) describes that measurement of

gelatinolytic activity in tumor tissues and its inhibition by MMP inhibitors. We have discussed this in the past with Lynn Matrisian, particularly as it relates to tumors for which repeated biopsies are feasible (e.g. head & neck).

Steve
Kysa A Meek

Kysa A Meek

08/15/2000 04:25 PM

To: Steven K Davidsen/LAKE/PPRD/ABBOTT@ABBOTT
cc:
Subject: MMP PD markers

Oops here are the markers:

The following biologic markers will be done on screening, Day22, month two, then every three months: VEGF, FGF, TNF1B and IL-8 plasma samples

We are planning to do these in conjunction with the tumor assessments-- CT or MRI scans.

Kysa

---------- Forwarded by Kysa A Meek/LAKE/PPRD/ABBOTT on 08/15/2000 04:23 PM ----------

Kysa A Meek

08/15/2000 04:18 PM

To: Steven K Davidsen/LAKE/PPRD/ABBOTT@ABBOTT
cc:
Subject: MMP PD markers

Steve,

I am working on the multiple dose protocol for the MMP. Would you please review this PD marker wording and let me know if there are other markers that we should examine? Are these appropriate for this compound?

I appreciate you input,

Kysa

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------

Steve Wittenberger
08/28/2000 03:09 PM

To: Steve King/LAKE/PPRD/ABBOTT@ABBOTT
cc: Clint Brooks/LAKE/PPRD/ABBOTT@ABBOTT, Dan W Norbeck/LAKE/PPRD/ABBOTT@ABBOTT, John M Leonard/LAKE/PPRD/ABBOTT@ABBOTT, Steven K Davidsen/LAKE/PPRD/ABBOTT@ABBOTT, John F Bauer/LAKE/PPRD/ABBOTT@ABBOTT, David M Brown/LAKE/PPRD/ABBOTT@ABBOTT, Gopi N Menon/LAKE/PPRD/ABBOTT@ABBOTT, Louise M Dube/LAKE/PPRD/ABBOTT@ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, Diane L D'Amico/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Azmi A Nabulsi/LAKE/PPRD/ABBOTT@ABBOTT, Perry D Nisen/LAKE/PPRD/ABBOTT@ABBOTT, James Steck/LAKE/PPRD/ABBOTT@ABBOTT, William M Bracken/LAKE/PPRD/ABBOTT@ABBOTT, David A Riley/ASHLAND/HPD/ABBOTT@ABBOTT
Subject: ABT-518 process report

Please find enclosed the process report describing the synthesis of ABT-518. A total of 5.89 kg of material was prepared under c-GMP guidelines. A 1.75 kg portion of this was used to support pre-clinical one-month toxicological studies. The remainder was recrystallized in the SPD R8 Special Lab and 3.80kg was made available for use in the planned Phase I multiple rising dose study.

The process consists of six synthetic steps which produce bulk drug in 50% overall yield as a white crystalline powder. The key reactions in the synthesis are: (a) the lithium sulfone anion addition to (R)-methyl-O-isopropylidine glycerate to produce the intermediate ketone in good yield and high enantiomeric excess, (b) the diastereoselective Michael addition of N-hydroxylamine to the vinyl sulfone, and (c) the formylation reaction that produces ABT-518 in high yield and excellent purity.

518 PR cover.doc ABT-518 PR.doc

SJW

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------

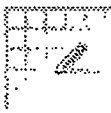
Robert Hansen
09/01/2000 03:31 PM

To: Walid Awni/LAKE/PPRD/ABBOTT@ABBOTT, John F Bauer/LAKE/PPRD/ABBOTT@ABBOTT, William M Bracken/LAKE/PPRD/ABBOTT@ABBOTT, Diane C Bronson/LAKE/PPRD/ABBOTT@ABBOTT, Robert A Carr/LAKE/PPRD/ABBOTT@ABBOTT, Steven K Davidsen/LAKE/PPRD/ABBOTT@ABBOTT, Tawakol A El-Shourbagy/LAKE/PPRD/ABBOTT@ABBOTT, Karla Fischer/LAKE/PPRD/ABBOTT@ABBOTT, Tamara L Garavalia/LAKE/PPRD/ABBOTT@ABBOTT, Julie A Garren/LAKE/PPRD/ABBOTT@ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Thomas C Harris/LAKE/AI/ABBOTT@ABBOTT, Dean Hickman/LAKE/PPRD/ABBOTT@ABBOTT, Rebecca S Hoffman/LAKE/PPRD/ABBOTT@ABBOTT, Steve King/LAKE/PPRD/ABBOTT@ABBOTT, Carmine Lanni/LAKE/PPRD/ABBOTT@ABBOTT, Michelle A Long/LAKE/PPRD/ABBOTT@ABBOTT, Lisa A Lux/LAKE/PPD/ABBOTT@ABBOTT, Kennan C Marsh/LAKE/PPRD/ABBOTT@ABBOTT, Diane M Medina/LAKE/PPRD/ABBOTT@ABBOTT, Kysa A Meek/LAKE/PPRD/ABBOTT@ABBOTT, Sherry J Morgan/LAKE/PPRD/ABBOTT@ABBOTT, Azmi A Nabulsi/LAKE/PPRD/ABBOTT@ABBOTT, Anil N Namboodiripad/LAKE/AI/ABBOTT@ABBOTT, Chudy I Nduaka/LAKE/PPRD/ABBOTT@ABBOTT, Robert ODea/LAKE/PPRD/ABBOTT@ABBOTT, Anita P Bakker/LAKE/PPRD/ABBOTT@ABBOTT, Matthew J Rieser/LAKE/PPRD/ABBOTT@ABBOTT, Stanley A Roberts/LAKE/PPRD/ABBOTT@ABBOTT, Lori V Rountree/LAKE/PPRD/ABBOTT@ABBOTT, Yeshwant D Sanzgiri/LAKE/PPRD/ABBOTT@ABBOTT, James Steck/LAKE/PPRD/ABBOTT@ABBOTT, Javier F Suarez/LAKE/CAPD/ABBOTT@ABBOTT, Steven E Townsend/LAKE/PPRD/ABBOTT@ABBOTT, Steve Wittenberger/LAKE/PPRD/ABBOTT@ABBOTT, Jim Looman/HOOFDDORP/AI/ABBOTT, Gordon Boyd/MAIDENHEAD/AI/ABBOTT@ABBOTT, Jan Peter de Geus/HOOFDDORP/AI/ABBOTT
cc:
Subject: MMPI Transition Strategy Paper

Attached is the Transition Strategy Paper for the MMPI compound, ABT-518

ABT-518 Transition Strategy.d

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------



Robert Hansen
09/27/2000 08:41 AM

To: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT
cc:
Subject: Marimastat/ovarian

---------- Forwarded by Robert Hansen/LAKE/PPRD/ABBOTT on 09/27/2000 08:41 AM ----------

Steven K Davidsen 09/27/2000 06:01 AM

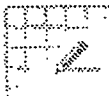
To: Perry D Nisen/LAKE/PPRD/ABBOTT@ABBOTT, Azmi A Nabulsi/LAKE/PPRD/ABBOTT@ABBOTT, Saul H Rosenberg/LAKE/PPRD/ABBOTT@ABBOTT, Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT
cc:
Subject: Marimastat/ovarian

As expected....

Date: Wednesday, September 27, 2000
Source: Business Wire

OXFORD, England--(BUSINESS WIRE) via NewsEdge Corporation -- British Biotech (NASDAQ:BBIOY) announces the results of Study 186, a clinical trial of the oral matrix metalloproteinase inhibitor, marimastat. Patients enrolled into the study had advanced ovarian cancer that had failed to respond to at least one prior treatment with carboplatin. The trial was designed to study the effect of marimastat, when given in combination with carboplatin, on these patients.
Treatment with the combination of carboplatin and marimastat showed no statistically significant advantage over carboplatin alone in either primary or secondary endpoints.
This news release contains forward-looking statements which reflect the Company's current expectation regarding future events. Forward-looking statements involve risks and uncertainties. Actual events could differ materially from those projected herein and depend on a number of factors including the success of the Company's research strategy, the applicability of the discoveries made therein, the successful and timely completion of clinical studies and the uncertainties related to the regulatory process.

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------



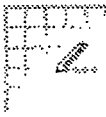
Steve Wittenberger
09/29/2000 01:41 PM

To: Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT
cc: Steve King/LAKE/PPRD/ABBOTT@ABBOTT
Subject: ABT-518 supplies

Thanks for coming over yesterday. I wanted to get a little more information on the planned phase two studies. There were two I believe, but you did not have the bulk drug requirements on hand If you would pass those estimates on to me, I will put together a plan for the next 518 campaign. I would like to make enough to re-supply the first multiple rising dose study, the "new" phase 1 study and both the phase two studies if that is possible and "bugetable". Thanks.

SJW

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:42 AM ----------



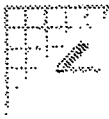
Steve Wittenberger
10/03/2000 04:56 PM

To: Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT
cc: Steve King/LAKE/PPRD/ABBOTT@ABBOTT
Subject: ABT-518 supplies

Any progress on getting these estimates?

SJW

---------- Forwarded by Steve Wittenberger/LAKE/PPRD/ABBOTT on 10/03/2000 04:54 PM ----------



Steve Wittenberger
09/29/2000 01:41 PM

To: Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT
cc: Steve King/LAKE/PPRD/ABBOTT@ABBOTT
Subject: ABT-518 supplies

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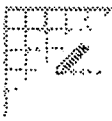
SJW

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:43 AM ----------



Steve King
10/03/2000 05:03 PM

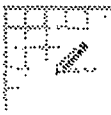
To: Robert Hansen/LAKE/PPRD/ABBOTT@ABBOTT, Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT
cc: Steve Wittenberger/LAKE/PPRD/ABBOTT@ABBOTT
Subject: ABT-518 supplies

Bob, Sue,

If you could shoot study design that would probably be enough.....x studies, y patients, z months. We can make some guesstimates from there based upon rising dose study.

thanks.
Steve(s)

---------- Forwarded by Steve King/LAKE/PPRD/ABBOTT on 10/03/2000 05:01 PM ----------



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10/03/2000 04:56 PM

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cc: Steve King/LAKE/PPRD/ABBOTT@ABBOTT
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SJW

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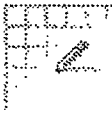

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cc: Steve King/LAKE/PPRD/ABBOTT@ABBOTT
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SJW

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:43 AM ---------

Jackie A Schroeder 10/05/2000 02:57 PM

To: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT, Kysa A Meek/LAKE/PPRD/ABBOTT@ABBOTT
cc:
Subject: CDA - Professor Beijnen

We do have a CDA on file for Professor Beijnen at The Netherlands Cancer Institute It is good until March of next year.

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:43 AM ---------

Azmi A Nabulsi
10/07/2000 07:18 AM

To: Susan M Glad/LAKE/PPRD/ABBOTT
cc:
Subject: Re: ABT-518 supplies

let us discuss when Bob returns.

---------- Forwarded by Susan M Glad/LAKE/PPRD/ABBOTT on 10/19/2000 11:43 AM ---------

Todd J Janus
10/11/2000 08:57 AM

To: Susan M Glad/LAKE/PPRD/ABBOTT@ABBOTT
cc:
Subject: ABT-518

I need to get up to speed on this ASAP thus we will need the following(I know about Diane's role but do not know when the announcement will be made and when I can peak with her, please forward when appropriate) Since this is the first time we will have worked together I especially need know what is expected of me, what I need to worry about , what I need to do to help and how you want me to dovetail into the group, perhaps we can discuss this tomorrow at the meeting Also I need:

1) all reports, documents, white papers, forms, meeting minutes, discussions, e-mails, etc. on 5-8 related to in vitro experiments, in vivo experiments, DDC documents, etc. If in PDF files would be great! Todd: I believe that everything pertaining to 518 with the exception of e-mails is currently on the L-drive in a cancer folder. It will take some time to generate the e-mails.

2) Who can I talk to about the safety meeting? I have never been to one, am unsure of the objective, what documents need to be sent to the committee and have no idea what is to be presented, what is to be

discussed, by whom and for how long. Also we need to set up practice sessions for the presentations, identify whom will speak for how long and make sure we have all the bases covered Bill Bracken and Reid speak to the toxicology, Kennan Marsh and Stan Roberts discuss preclinical PK/metabolism, Bryan Cox speaks to safety pharmacology, and Azmi lays out the clinical protocol and how we plan on monitoring for safety issues seen during development The past 2 that I attended did not require practice seesions.

3) We need the updated protocol, we can not wait any further for investigator comments if we have not received them. I am setting up a meeting for tomorrow where we can address the protocol Kysa is e-mailing Schellens to see if or when he sent his comments.

4) What is the status of the investigators brochure - we need this complete no later than 20 October to allow time for review by the committee. I'll give you an update tomorrow.

5) What is the status of drug supply, regulatory issues and the like about shipping product? 25 mg caps to be shipped to IDC on 12/4 but we are trying to get them shipped earlier. Regulatory issues under control.

6) Do we plan real time pK data? I heard this was going on in previous studies if so we need to know how that will be handled and when we will get the info. I think I need to sit down with Bob Carr. The method is being transferred to Schellen's shop where they will perform the assay. For TSP we decided not to have PK an escalation criteria and I suspect we would want the same for this study.

7) Sorry if this sounds like a barrage but I need to get up to speed- is there anything else I need to know that I have forgotten?

- There is an MMPI Transition meeting tomorrow from 3-5 where your introduction to the clinical team will be made.
- We have just heard that there could be a small tox concern I know very little about the specifics but Bracken will explain to Azmi who will explain to you. Reportedly the finding was only seen at the highest dose level in rats (400 mg/kg/day).

thanks

tjj

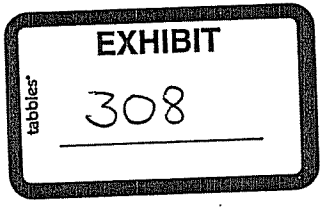
EXHIBIT 308

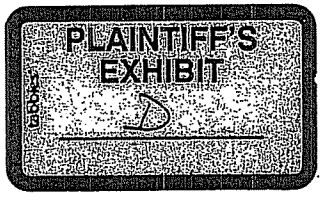
JULY 2000 - "Top" Issues

Key Issues/Decisions/Events

Area	Issue/Decision/Event	Progress
Depacon Rapid Infusion (M98-938)	Redacted	
ABT-518 Competitive Environment	As several competitors are in Phase II/III, ABT-518 product profile will need to demonstrate advantage over the other compounds (i.e. safety/efficacy)	Ongoing analysis and comparison of competition throughout transition. ABT-518 has the potential to be the best in class compound. Pfizer (Agouron) announced 8/4/00 that they were stopping Phase III trials of prinomastat in advanced prostate and NSCLC because "primary efficacy objectives were not met". They are continuing trials in less advanced tumors, e.g., esophagus, melanoma, breast, glioma, and NSCLC, and will start trials in two additional tumor types. Efficacy was shown with marimastat in less advanced gastric cancer. Both compounds were hindered by dose-limiting joint toxicity.
ABT-627	Submission of the End-of Phase II package to Regulatory Agencies is delayed pending initial ECG analyses projected to be completed August 28. Meetings with the agencies will be scheduled after completion of the ECG interpretation.	
ABT-773 HPD	The initial development of an IV formulation has been completed but funding has not resolved between PPD and HPD. HPD has decided to fund the clinical manufacturing runs for the Phase I IV formulation study. This is planned for August 29th.	The IV program is currently on hold. HPD does not have funds for the year 2000. Discussions are underway within the Franchise to identify funding. HPD has decided to fund the clinical manufacturing of IV supplies at the end of August. PPD and HPD continue to pursue funding options to complete the Phase I IV study.

Redacted





JULY 2000 - "Top" Issues

Key Issues/Decisions/Events

Area	Issue/Decision/Event	Progress
ABT-980 (Fiduxosin) Clinical		
Toxicology		

Redacted

Pharmaceutical Products Research & Development

2000 Discovery Development Candidate (DDC) Target Dates
JULY 2000

PROJECT/COMPOUND	THERAPEUTIC TARGET	PROBABILITY	TARGETED REVIEW DATE CURRENT MONTH	PRIOR MONTH
Redacted				
Anti-Mitotic	Cancer	Complete	March 9	March 13 March 9
Quinolone (In-house)	Anti-infective	>25%	December 15, 2000	December 12, 2000
Anti-Mitotic (7010)	Cancer	Complete	March 9	March 9

STATUS OF PAST CANDIDATES NOT FUNDED

PROJECT/COMPOUND	THERAPEUTIC TARGET	ABT #	STATUS
Redacted			
Endothelin #1	Prostate Cancer/Cardiovascular	ABT-627	Phase II clinical trials
Redacted			
ABT-773 Backup #1=(ABT-797)	Anti-infective	ABT-797	On hold pending ABT-773 results

NOTE: CHANGES FROM PRIOR

PHARMACEUTICAL PRODUCTS RESEARCH & DEVELOPMENT
GLOBAL AI SPLIT
($MILLIONS)

Ongoing Development Programs	2000 PLAN Global	2000 PLAN Domestic	2000 APU Global	2000 APU Domestic	Key Unfunded Programs
NEUROLOGY					
Cholinergic Channel Modulator	15.0	...	15.0	...	8.0 A.
ANTI IFECTIVE					
Ketolide	71.3	...	74.1	...	5.7 B.
Quinolone	14.0	...	6.8	...	
UROLOGY/CARDIOLOGY					
HIV					
CANCER					
Endothelin	6.0	...	8.0	...	5.0 E.
Metalloprotease (MMPI)	5.0	...	5.0	...	...
Farnesyltransferase (FTI) #2	3.8	...	...	...	...
Anti-Mitotoc	5.0	...	3.0	...	...
Discovery					
Total PPD (Without Risk)					
Risk/Affordability					
Total PPD (With Risk)					
[redacted]					
[redacted]					

D477\

EXHIBIT 67

EXHIBIT
tabbies 67

PLAINTIFF'S EXHIBIT
tabbies 7

February 2001 — ABT-518

Feb-01 — **ABT-518 (Matrix Metalloproteinase Inhibitor)**

Franchise	Dev. Status	Brand Name	Generic Name	Patent Exp.	Indication(s)
Oncology	Phase I	TBD	TBD	2018	Solid tumors such as breast, non-small cell lung, ovarian and colorectal cancers; non-Hodgkin's lymphoma

Description

ABT-518 is a metalloproteinase inhibitor that selectively targets MMP-2 and MMP-9, metalloproteinases that have been implicated in the progression of cancer.

In preclinical studies ABT-518 inhibits tumor growth in a variety of murine tumor models when administered alone, or acts synergistically with cytotoxic agents. ABT-518 also blocks blood vessel formation in a murine angiogenesis model.

U.S. Market

Unit	Value	CAGR	Unmet Need/Key Market Drivers	Key Competitors/Factors to Market
TRX	NA		Despite major advances in our understanding of the molecular events that underlie cancer, the disease remains the second leading cause of death in the US, with more than 550,000 cancer deaths last year alone. Today advanced cancer is primarily treated with a combination of cytotoxic agents that typically offer limited efficacy coupled with debilitating side effects. New therapies that demonstrate a clinically significant improvement in efficacy (survival or time to disease progression as a surrogate to survival) and limited side effects have significant market opportunities.	MMPIs (e.g. BMS-275291, prinomastat), Taxanes, Taxol, Taxotere and generic paclitaxel. Other cytotoxics such as Camptosar, Navelbine, Campotecan, Hycamtin, 5-FU, Xeloda, Platinol and Paraplatinol. Antibody therapies such as Herceptin and Rituxan. Emerging cytostatic agents such as tyrosine kinase inhibitors (e.g. Iressa, EU5416), FTIs, and other angiogenesis inhibitors (e.g. endostatin, angiostatin). The competitors will vary depending upon the cancer type(s) where ABT-518 demonstrates efficacy.
Sales	$3,500 MM	14% global		

Ex-U.S. Market

Unit	Value	CAGR	Unmet Need/Key Market Drivers	Key Competitors/Factors to Market
TRX	NA		There are significant unmet needs in cancer Ex-US, where cancer is the leading cause of death in Japan and the second leading cause of death in Europe. Physicians are looking for agents that demonstrate improved efficacy when used either as single agents or in combination with existing regimens.	Competitors are similar to those in the US. Government agency analyses for cost effectiveness of the therapy is important for reimbursement in some countries.
Sales	$4,700 MM	14% global		

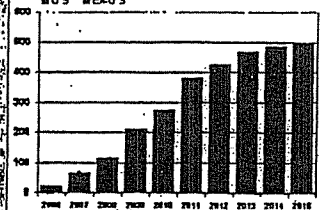
Development

Cost for NDA	DDC Est.	Thru 2000	YTD	Proj.	2001 Budget	Var.	2002	2003	2004	2005	Post	Total
Chemistry	$0.0	$1.8	$0.3	$3.2	$2.2	$0.0	$19.0	$21.0	$19.0	$16.0	TBD	$78.8
CMC	$0.0	$1.8	$0.1	$2.3	$2.2	$0.0	$6.0	$11.0	$4.0	$4.0	TBD	$26.0
Drug Safety	$0.0	$1.6	$0.6	$2.3	$3.3	$0.0	$6.0	$4.0	$3.0	$2.0	TBD	$21.1
Other	$0.0	$0.4	$0.1	$0.7	$0.7	$0.0	$3.0	$5.0	$3.0	$1.0	TBD	$13.1
TOTAL	$0.0	$5.6	$1.1	$7.4	$7.4	$0.0	$34.0	$36.0	$29.0	$23.0	TBD	$139.0

	DDC ($000)	LSE	Actual
Start of Tox			2Q2000
Phase I		1Q2001	
Phase II		3Q2002	
Phase III		4Q2003	
Last Pt Last Visit			
US, EU, Japan Filing		4Q2005	
US, EU, Japan Approval		2Q2006	

Commercial

Base Case Forecast ($MM)



Product Profile (Efficacy, Safety, Convenience)

	Code	Price Impact
Safety/AE	Addition of ABT-518 to cytotoxic regimen does not add significant side effects; side effects are similar to current gold standard	
Convenience	Oral, daily therapy	
Efficacy	Initial indication: Approved for use in second line regimen in advanced patients in one mechanism-type cancer (e.g. breast, NSCLC, ovarian, NHL, or colorectal); in combination with cytotoxic therapies demonstrates clinically significant improvement in survival or time to tumor (or disease) progression compared to current gold standard in second line therapy	
Efficacy	Second indication (in year 3): Approved as a first line therapy in advanced patients in the same tumor type as initial indication with equivalent or marginally better efficacy compared to current gold standard	
Efficacy	Third indication (in year 5): Approved as a second line therapy in a distinct tumor type, with equal or marginally better efficacy than current gold standard	
Other	US: For patients with commercial insurance, ABT-518 will be covered with a minimal co-pay ($20), Medicare will not reimburse for ABT-518 as a self administered medication; 75% patient compliance	

Commercial Profile	U.S.	Ex-U.S.
Launch Date	Q3 2009	Q1 2007
Price per Day of Launch (AWP)	$2,000.00 Similar to cancer, HIV, and transplant drugs	$4,500.00 Similar to cancer drugs
Sales Peak @ peak sales ($MM)	$7	$4
Share @ peak sales (SMM)	15	15
COGS @ launch, @ peak)	90% $/MM	90% $/MM
Market/Extension/Other	Assumes 2% annual price increases	

Financial Summary	U.S. ($MM)	Ex-U.S. ($MM)
Peak Sales ($MM)	$307	$189
Peak Standard Margin ($MM)	$275	$170
Peak Standard Margin (%)	89.6%	89.9%
Pre-Tax NPV @ 12.5% (global)	$484	

Next Go/No-Go — End of Phase I (early 2002)

Business Rationale — With ABT-518, ABT-510 and ABT-627, Abbott can establish itself as a clear leader in angiogenesis inhibition with 3 anti-angiogenesis drugs that act by alternative mechanisms. The MMP-2 and -9 selectivity should allow for a larger therapeutic window and thus the potential for higher efficacy and lower toxicity than other MMPIs such as marimastat and prinomastat.

1 of 1

Leeden EXHIBIT 37
FOR I.D. 4-26-07 JMK

February 2001 — ABT-518

Monthly Highlights – Key Project Progress

- Study initiation visits were conducted on 2/14 and 2/15.

Next Quarter's Key Progress Markers

Key Progress Marker	Target Date
• First patient enrolled	3/12
• Preliminary results from 6-week rat hepatotoxicity study	3/31
• Pre-IND meeting with FDA	6/1
• Preliminary results from 3-month rat chronic toxicity study	6/30

Key Project Issues and Risks

Risk or Issue	Potential or Known Impact (Check all that apply to each risk or issue)	Strategy	Area	Resolution Date Planned / Actual
Identification of FDA requirements for cytostatic agents in oncology drug development.	☐ Cost ☐ Time ☐ Profile ☑ Regulatory	Phase I IND study to Transition program to solicit FDA input.	Clinical	6/1/01
Key tox finding was hepatotoxicity in one-month rat study. *In-vitro* and *in-vivo* data indicate a potential for mechanism based drug interactions.	☐ Cost ☐ Time ☑ Profile ☑ Regulatory	The Phase I first-in-man protocol has been designed to address these issues. A 6-week tox and metabolism studies have been completed. Results are under review. A 3-month rat toxicity study is ongoing.	Toxicology/ Metabolism	7/1/01

Risk or Issue	Potential or Known Impact (Check all that apply and describe impact)	Strategy / Progress	Lead / Responsibility	Resolution Date Planned / Actuals
As several competitors are in Phase II/III, ABT-518 product profile will need to demonstrate advantage over the other compounds (i.e., safety/efficacy)	☐ Cost ☐ Time ☑ Profile ☐ Regulatory	Ongoing analysis and comparison of competition throughout transition. ABT-518 has the potential to be the best in class compound. Pfizer (Agouron) announced 8/4/00 that they were stopping Phase III trials of prinomastat in advanced prostate and NSCLC because "primary efficacy objectives were not met". They are continuing trials in less advanced tumors, e.g., glioma and NSCLC, and will start trials in two additional tumor types. Efficacy was shown with marimastat in less advanced gastric cancer, but British Biotech announced on 9/27/00 that marimastat in combination with carboplatin was no better than carboplatin alone in advanced ovarian cancer. **Marimastat development was discontinued on 2/15/01.** Both the Pfizer compound and British Biotech's compound are hindered by dose-limiting joint toxicity.	Competitive Environment	
	☐ Cost ☐ Time ☐ Profile ☐ Regulatory			

Key Activities

Commercial

Activity	LBE	Actual
Market research to assess commercial potential of cancer types, both US and Ex-US.....	4/2001	
Assessment of patient compliance (for revision of forecast)	3/2001	
Assessment of off-label vs. spillover use (for revision of forecasts)	3/2001	
Assessment of cancer market growth (for revision of forecasts)	4/2001	
Assist with advisory planning	4/2001	
Development of brand and generic names	Late 2001	

Formulation

Plan Date: 3/2000

Activity	Plan	Actual
Phase I Formulation	10/2000	
Phase II Formulation		
Formulation for Bio Study		
Phase III Clinical Supplies Manufactured		
NDA Lots (3) Completed		
Completion of 1 Year Stability for NDA		
Formulation Peer Review		

Drug Substance

Plan Date: 3/2000

Activity	KG	Plan	Actual	Actual Projected Cost/kg
Chem Scien (GLP)	3.0/1.7	6/2000	6/16/00	$133,300
Chem Scien (GMP)	2.0/3.8	6/2000	6/29/00	$133,300
Chem Scien	15.0	6/2001		
SPD				
SPD				
SPD				
Demo Lot				
NDA Lot #1				
NDA Lot #2				
NDA Lot #3				
Validation Lot				

Toxicology

Plan Date: 3/2000

Toxicology Activity	Planned Start	Actual Start Date	Report Completed
Gene Toxicology	5/2000		
Acute Studies	5/2000		
2-Week Monkey (non-GLP)	12/1999	12/14/99	
1-Month Rat (non-GLP screening)	12/1999	12/14/99	
1 Month Rat (GLP)	6/2000	6/27/00	
1 Month Monkey (GLP)	6/2000	6/29/00	
3 Month Rat	1/2001	1/2/01	
3 Month Mouse MTD			
SEG I and SEG II			
SEG III Rat (post natal development)			
6 Month Rat			
1 Year Monkey			
Carcinogenicity (2 yr) Rat			
Carcinogenicity (2 yr) Mouse			

All Clinical Studies:

Protocol Number	Phase	Study Name	Start 1st Pt. Dosed	End (Last CRF In)	Patients Target	Patients Current
M00-235	I	MD Study in cancer patients	2/28		40	
TBD	I	IND Study			20	

Protocol Number	Phase	Study Name	Start 1st Pt. Dosed	End (Last CRF In)	Patients Target	Patients Current

Ongoing Clinical Studies (List first-time in man, Phase II Dose-Ranging and Pivotal Trials)

Protocol:	**M00-235 - Phase I MD in cancer patients**	**MXX-XXX – TITLE**
Objective:	**Determine MTD and safety profile in cancer patients**	
ABT-518 Doses:	**25, 50, 100, 200, 400, 800, 1200, 1600, 2000 mg/day**	
Comparator Doses:	**N/A**	
Target Enrollment:	**40**	
Status:	**Study initiated, clinical supplies delivered**	
Major Findings:		

(Author: Double click on chart to edit)